薬物代謝工学分野　Division of Metabolic Engineering

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◇研究目的

薬物代謝工学分野は和漢薬の薬効、毒性発現に関与する代謝系の分子生物学的研究を発展させることを設置目的とし、(1) 和漢薬の薬効発現に関与する腸内細菌の役割の解明、(2) 酵素免疫測定法やLC/MS/MSによる和漢薬活性成分の薬物動力学的研究、(3) AIDS、C型肝炎ウイルスに有効な天然薬物の探索、(4) 霊芝、樟芝などの担子菌類の薬効評価、(5) 内分泌調節作用を有する和漢薬の研究 などを研究テーマとしている。

◇研究概要

Ⅰ) 和漢薬の薬効発現に関与する腸内細菌の役割の解明

1) リグナン arctigenin の脱メチル化に関与するヒト腸内細菌 *Eubacterium* sp. ARC-2 を単離した。本菌は *Eubacterium limosum* と近縁種であり、芳香環に付いたメトキシ基をフリー水酸基にする活性を有していた。基質特異性が低く、広く天然物の脱メチル化の目的で利用できる可能性が大きい。

2) Enterodiol や enterolactone の前駆体の脱ヒドロキシ反応に関与するヒト腸内細菌 *Eggerthela* sp. SDG-2 および Strain ARC-1 を単離同定した。前者は (+)-dihydroxyenterodiol (DHEND) を (+)-enterodiol (END)に (-)-dihydroxyenterolactone (DHENL)を (-)-ENL に変換する活性を有していた。一方 後者は これらのエナンチオーマのみ 基質とし、脱ヒドロキシ反応に関与した。

Ⅱ) 酵素免疫測定法や LC/MS/MS による和漢薬活性成分の薬物動力学的研究

berberine をラットに経口投与し、血中に berberrubine、thalifendine、demethylene berberine、jatorrhizine およびそのBグルクロン酸抱合体を検出した。通常動物と疑似無菌ラットの比較から berberine の代謝は肝臓で行なわれるが、代謝物の腸肝循環も重要な役割を果たしていることを明らかにした。

Ⅲ) AIDS、C 型肝炎ウイルスに有効な天然薬物の探索

中国雲南省で購入した薬物 93 種のC型肝炎ウイルス由来の RNA 依存性 RNA 合成酵素阻害を検討した結果、*Tripterygium hypoglaucum* が強い阻害を示し、このエキスからA環が芳香環化しアルデヒド基を有する demethylzeylasteral を活性成分として単離した (IC_{50} = 7.4μM)。

Ⅳ) 霊芝、樟芝などの担子菌類の薬効評価

ベトナム産 *Ganoderma colossum* からA環の開裂した新規トリテルペン数種を単離、構造決定した。

Ⅴ) 内分泌調節作用を有する和漢薬の研究

当帰芍薬散を卵巣摘出ラットに経口投与し 子宮重量の増加、血中エストロゲン濃度の上昇がみられ、これら女性ホルモン様作用のメカニズムの検討を行なった。

◇著書

1) 服部征雄：薬用植物・生薬の開発，佐竹元吉 監修．（服部分担），シーエムシー出版．

2) 服部征雄：コーヒーの科学と機能，グュエン・ヴァン・チュエン，石川俊次 共編（服部分担），アイ・ケイコーポレーション．

◇原著論文

1) **Gao J. J., Hirakawa A., Min B. S., Nakamura N., Hattori M.: *In vivo* antitumor effects of bitter principles from the antlered form of fruiting bodies of *Ganoderma lucidum*. *J. Nat. Med.*, 60: 42-48, 2006.**

Abstract: Two triterpene fractions and a single ganoderma alcohol obtained from an antlered form of the fruiting bodies of *Ganoderma lucidum* were examined for their antitumor effects on the growth of inoculated mouse Lewis lung carcinoma in mice by intraperitoneal administration. The ganoderma alcohol fraction significantly suppressed the tumor growth at doses of 50 and 100 mg/kg in the treatment period, and even after the administration, showing antitumor activity with a *T/C* value of 70.6% at a dose of 100 mg/kg. On the other hand, no obvious activity was shown at each dose in the ganoderma-acid-fraction-treated groups. Furthermore, ganoderiol F, which exhibited the strongest cytotoxicity against four tumor cell lines among five ganoderma alcohols examined, remarkably inhibited the tumor growth, accounting for 63.7% and 78.7% of control group at a dose of 5 mg/kg, 54.1% and 63.0% at a dose of 10 mg/kg, and 47.7% and 53.9% at a dose of 20 mg/kg in and after the administration period, respectively, in a dose-dependent manner. These results suggest that the antitumor effects of bitter principles in *G. lucidum* are mainly due to ganoderma alcohols.

2) **Sun Q. Z., Chen D. F., Ding P. L., Ma C. M., Kakuda H., Nakamura N., Hattori M.: Three new lignans, longipedunins A−C, from *Kadsura longipedunculata* and their inhibitory activity against HIV-1 protease. *Chem. Pharm. Bull.*, 54: 129-132, 2006.**

Abstract: Three new lignans, logipedunins A (**1**), B (**2**) and C (**3**), together with three known compounds, benzoyl-binankadsurin A (**4**), acetyl-binankadsurin A (**5**) and schisanlactone A (**6**), were isolated from *Kadsura longipedunculata*. Their structures and stereochemistry were determined by spectral and single-crystal X-ray analyses. Compounds **1** and **6** showed appreciable inhibitory activity against HIV-1 protease with IC_{50} values of 50 and 20 μM, respectively.

3) **Han H. F., Hirakawa A., Zuo F., Nakamura N., Hattori M.: Quantitative determination of maleic and succinic acid derivatives in the mycelium of *Antrodia cinnamomea*. *J. Trad. Med.*, 23: 19-23, 2006.**

Abstract: For the purpose of quantitative determination of novel maleic acid and succinic acid derivatives, antrodins A−E, in the mycelium of *Antrodia cinnamomea*, a high-performance liquid chromatography (HPLC) method was applied to separation of these compounds under the conditions, where the mobile phase was a linear gradient of 1% AcOH/H_2O-CH_3CN, the flow rate was 1.0 ml/min and the detecting wavelength was 235 nm, using an ODS column. The relative standard deviations of this method were less than 4.6% and 4.1% (n=5) for interday and intraday assays, respectively. A good linear correlation was obtained in a range of 0.1 (or 0.2) μg – 1.2 μg. The recoveries of antrodins A, B, C, D and E were 99.8, 102.9, 101.0, 100.5 and 99.9%, respectively. This method was rapid, accurate and suitable for the quantitative determination of maleic acid and succinic acid derivatives in the mycelium of *Antrodia cinnamomea*.

4) **Han H. F., Nakamura N., Zuo F., Hirakawa A., Yokozawa T., Hattori M.: Protective effects of a neutral polysaccharide isolated from the mycelium of *Antrodia cinnamomea* on *Propionibacterium acnes* and lipopolysaccharide induced hepatic injury in mice. *Chem. Pharm. Bull.*, 54: 496-500, 2006.**

Abstract: Mycelia of *Antrodia cinnamomea* were extracted with chloroform and hot water. A neutral polysaccharide named *ACN2a* separated from the water extract was purified using 10% CCl_3COOH, and repeated column chromatography on HW-65 and DE-52 cellulose. Its structure was determined by chemical and spectroscopic analyses. *ACN2a* was composed of Gal, Clc, Fuc, Man and GalN (in the ratio 1 : 0.24 : 0.07 : 0.026 : faint), in which an α-D-(1→6)-Gal linkage accounted for 73% of all linkages. The ratio of branch points was about 16% of the total residual numbers, and branches were attached to C-2 of galactosyl residues of the main chain. *ACN2a* had an average molecular weight of 12.9×10^5 Daltons, $[\alpha]_D^{25}$=+115° (*c*=0.44, H_2O); $[\eta]$ =0.0417dl · g^{-1}, *Cp*=0.2663 cal/(g · ℃). The hepatoprotective effect of *ACN2a* was evaluated using a mouse model of hepatic injury that was induced by *Propionibacterium acnes* (*P. acnes*) and lipopolysaccharide (LPS). The administration of *ACN2a* (0.4, 0.8 g/kg/d, p.o.), significantly prevented increases in serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) enzyme activities in mice treated with *P. acnes*-LPS, indicating hepatoprotective activity *in vivo*.

5) **Jo M., Nakamura N., Kakiuchi N., Komatsu K., Qui M. H., Shimotohno K., Shimotohno K., Hattori M.: Inhibitory effect of Yunnan traditional medicines on hepatitis C viral polymerase. *J. Nat. Med.*, 60: 217-224, 2006.**

Abstract: For the purpose of developing novel antihepatitis C virus (HCV) agents from natural resources, 93 Yunnan crude drugs were screened for their inhibitory effects on RNA-dependent RNA polymerase (RdRp) of HCV. Although 71 methanol extracts and 50 water extracts inhibited HCV-RdRp by more than 50% at a concentration of 50 μg/ml, the majority of them contained a high percentage of tannins. However, methanol extracts of *Plumbago zeylanica* (branch), *Maytenus fookerii* (leaf) and Huashidancha (Y61, branch and leaf), and water extracts of *Potentilla griffithii* (whole plant) and *Salvia yunnanensis* (underground part), having IC_{50} values of less than 10 μg/ml, showed less than 10% tannin content. In addition, from a methanol extract of *Tripterygium hypoglaucum* (root back), demethylzeylasteral was isolated as a strongly inhibitory substance againdt HCV-RdRp.

6) **Han H. F., Nakamura N., Hattori M.: Protective effects of an acidic polysaccharide isolated from fruiting bodies of *Ganoderma lucidum* against murine hepatic injury induced by *Propionibacterium acnes* and lipopolysaccharide. *J. Nat. Med.*, 60: 295-302, 2006.**

Abstract: Fruiting bodies of *Ganoderma lucidum* were extracted with chloroform followed by hot water, from which an acidic polysaccharide named GLAa was separated and purified using 10% CCl_3COOH followed by column chromatography on DE-52 Cellulose and Toyopearl HW-65. Chemical and spectroscopic analyses showed that GLAa was composed of Glc, Gal, Man and Fuc (1:0.013:0.009:0.024), in which β-D-(1 → 6)-Glc, β-D-(1 → 3)-Glc and β-D-(1 → 4)-Glc linkages comprised 34.9, 33.9, and 28.7% of the total linkages, respectively. The average molecular weight of GLAa was 12.5×10^5 Da and the optical rotation was $[\alpha]_D^{25℃}$= −9.1° ; *c* =0.55, H_2O. Uronic (mannuronic) acid accounted for 14.8% of the molecule, protein, 0.14% and nitrogen, 0.75%. The hepatoprotective effect of GLAa was evaluated using a mouse model in which hepatic injury was induced with *Propionibacterium acnes* and lipopolysaccharide (LPS). GLAa (0.4 and 0.8 g kg^{-1} day^{-1}, b.w., p.o.), significantly prevented increases in serum aspartate aminotransferase and alanine aminotransferase levels in mice exposed to *P. acnes*-LPS, indicating that GLAa has hepatoprotective activity *in vivo*.

7) **Zuo F., Zhao J., Nakamura N., Gao J. J., Akao T., Hattori M., Oomiga Y., Kikuchi Y.: Pharmacokinetic study of benzoylmesaconine in rats using an enzyme immunoassay system. *J. Nat. Med.*, 60: 313-321, 2006.**

Abstract: A highly sensitive enzyme immunoassay (EIA) system for quantitative determination of benzoylmesaconine (BM) in biological samples was developed. The sensitivity of an antiserum towards β-galactosidase (β-gal)-labeled antigen was in the range of 10^{-1}-10^{5} ng/ml of BM in rat serum. Under the same conditions, the antiserum had quite weak cross-reactivity with related alkaloids in the aconite tuber. The coefficients of variance (CV) of intra- and interday assays were 6.4 and 10.2%, and 3.4 and 14.8% in the presence of high and low concentrations, respectively, of BM in rat serum. The concentration versus time curve of BM after intravenous administration corresponded to a two-compartment model, and that after oral administration corresponded to a one-compartment model. Benzoylmesaconine was identified as two peaks in serum at 48 h after oral administration; consequently its area under the serum concentration-time curve ($AUC_{0\text{-}48}$) and mean residence time (MRT) values were significantly high. Hydrolysis by intestinal bacteria followed by intestinal reabsorption accounted for these values. One hour after the oral administration of 0.8, 0.2 and 0.05 mg/kg of aconitine (A) or mesaconitine (M), the concentrations of each and their respective metabolites benzoylaconine (BA) or BM in serum and spinal cord samples were investigated. The concentrations of the original compounds were lower than those of their metabolites at all three doses, bat the increase in metabolites was more obvious in the spinal cord than in serum.

8) **Zuo F., Nakamura N., Akao T., Hattori M.: Pharmacokinetics of berberine and its main metabolites in conventional and pseudo germ-free rats determined by liquid chromatography/ion trap mass spectrometry. *Drug Metabolism and Disposition*, 34: 2064-2072, 2006.**

Abstract: Berberine (Ber) and its main metabolites were identified and quantified using liquid chromatography/electrospray ionization/ion trap mass spectrometry. Rat plasma contained the main metabolites, berberrubine, thalifendine, demethyleneberberine, and jatrorrhizine, as free and glucuronide conjugates after p.o. Ber administration. Moreover, the original drug, the four main metabolites, and their glucuronide conjugates were all detected in liver tissues after 0.5 h and in bile samples 1 h after p.o. Ber administration. Therefore, the metabolic site seemed to be the liver, and the metabolites and conjugates were evidently excreted into the duodenum as bile. The pharmacokinetics of Ber and the four metabolites were determined in conventional and pseudo germ-free rats (treated with antibiotics) after p.o. administration with 40 mg/kg Ber. The $AUC_{0\text{-}limt}$ and mean transit time values of the metabolites significantly differed between conventional and pseudo germ-free rats. The amounts of metabolites were remarkably reduced in the pseudo germ-free rats, whereas levels of Ber did not obviously differ between the two groups. The intestinal flora did not exert significant metabolic activity against Ber and its metabolites, but it played a significant role in the enterohepatic circulation of metabolites. In this sense, the liver and intestinal bacteria participate in the metabolism and disposition of Ber *in vivo*.

9) **Ma C. M., Takeda S., Hibino S., Daneshtalab M.: Synthesis of peptidomimetic analogues of echinocandines. *Heterocycles*, 68: 721-732, 2006.**

Abstract: Novel peptidomimetic compounds with partial structures being the same as that of echinocandin B, a well known antifungal lipopeptide, have been synthesized. The structures of these compounds were confirmed by NMR and MS. The synthesized compounds were tested for their *in vitro* antifungal activity. The results suggested that the hydroxyproline-threonine section in the north-western position of the echinocadin is important for the activity.

10) **Cai S. Q., Wang R. F., Yang X. W., Shang M. Y., Ma C. M., Shoyama Y.: Antiviral flavonoid-type *C*-glycosides from the flowers of *Trollius chinensis*. *Chemistry & Biodiversity*, 3: 343-348, 2006.**

Abstract: Two new flavonoid-type *C*-glycosides, trollisin I (=(1*S*)-1,5-anhydro-1-[2-(3,4-dihydroxyphenyl)-5-hydroxy-7-methoxy-4-oxo-4*H*-[1] benzopyran-8-yl]-2-*O*-(2- methylbutanoyl)-D-glucitol; **1**) and its 2-*O*-benzoyl congener trollisin II (**2**), were isolated from *Trollius chinensis* Bunge, together with the two known compounds 2''-*O*-(2'''-methylbutanoyl)isoswertisin (**3**) and vitexin

galactoside (**4**). All compounds were identified by HR-ESI-MS and in-depth NMR-spectroscopic analyses. In antiviral assays, compound **3** was found to be moderately active towards influenza virus A.

◇総　説

1) Min B. S., Gao J. J., Hattori M.: Bitter principles from the fruiting bodies, cultural mycelia and spores of *Ganoderma lucidum*. *Phytochemistry,* 7 : 35-60, 2005. （前号未記載）
2) 服部征雄: 和漢薬と腸内細菌のかかわり. *Biophilia*, 2 (No.3) : 54-58, 2006.

◇学会報告　（*: 特別講演、シンポジウム、ワークショップ等）

1) 和田明穂, 左 風, 中村憲夫, 服部征雄 : 樟芝菌糸体に含まれるマイレン酸誘導体のラットにおける代謝と体内動態. 日本薬学会第 126 年会, 2006, 3, 28-30, 仙台.
2) 陳 琮湜, 趙 宇峰, 中村憲夫, 赤尾光昭, 垣内信子, 服部征雄 : Dihydroxyenterodiol の脱水酸基反応に関与する腸内細菌の単離とその特性について. 日本薬学会第 126 年会, 2006, 3, 28-30, 仙台.
* 3) Hattori M.: Recent researches on medicinal mushrooms –*Ganoderma lucidum* and *Antrodia cinnamomea*–. China-Japan Jointed Symposium on Natural Medicine –Recent Trends of Natural Medicine Researches, 2006, 4, 28-29, Nanjing, China.
4) Gao J., Hattori M.: Individual variation in human metabolism of arctiin to ENL, monitored by LC/MS/MS. China-Japan Jointed Symposium on Natural Medicine –Recent Trends of Natural Medicine Researches, 2006, 4, 28-29, Nanjing.
5) 近藤直子, 中村憲夫, 吉村千秋, 増山明弘, 高野俊明, 服部征雄 : 乳酸菌による植物リグナンの代謝. 第 10 回腸内細菌学会, 2006, 6, 1-2, 東京.
6) 服部征雄 : 漢方薬の薬効発現には腸内細菌が関与する. 医療薬学フォーラム 2006 新時代の医療薬学への澪つくし –医療と科学の懸橋を目指して–, 2006, 7, 15-16, 大阪.
7) Ma C. M., Kully M., Khan J. K., Daneshtalab M.: Synthesis and biological evaluation of a novel series of chlorogenic acid derivatives with promising antifungal activity. ICOB-5 & ISCNP-25 IUPAC International Conference on Biodiversity and Natural Products, 2006, 7, 23-28, Kyoto, Japan.
* 8) Hattori M.: Intestinal bacterial reactions associated with the efficacy of herbal drugs. 2006 The 6th International Symposium on Natural Medicine and Microflora (6th ISNMM), 2006, 8, 6-8, Korea.
9) Chung M. H., Hattori M.: Female hormone secretion of Toki-shakuyaku-san (Tang-Gui-Shao-Yao-San) and research on a related gene expression change, using ovariectomized rats. 2006 The 6th International Symposium on Natural Medicine and Microflora (6th ISNMM), 2006, 8, 6-8, Korea.
10) Gao J., Hattori M.: Individual variation in human metabolism of arctiin to enterolactone monitored by LC/MS/MS. 2006 The 6th International Symposium on Natural Medicine and Microflora (6th ISNMM), 2006, 8, 6-8, Korea.
11) Lee J. S., Hattori M.: Preventive effect of ergosterol peroxide isolated from *Phellinus linteus* grown on germinated brown rice on experimentally induced acute liver injury in mice. 2006 The 6th International Symposium on Natural Medicine and Microflora (6th ISNMM), 2006, 8, 6-8, Korea.
12) Suzuki S. Chung M. H., Hattori M.: Estrogenic action of Toki-Shakuyaku–San (Tnag-Gui-Shao-Yao-San) in retirement female ovariectomized rats. 2006 The 6th International Symposium on Natural Medicine and Microflora (6th ISNMM), 2006, 8, 6-8, Korea.
13) Jin J. S., Zhao Y. F., Nakamura N., Akao T., Kakiuchi N., Hattori M.: Demethylation of arctigenin by a human intestinal bacterium, *Eubacterium* sp. ARC-2. 2006 The 6th International Symposium

on Natural Medicine and Microflora (6th ISNMM), 2006, 8, 6-8, Korea.
14) 高 江静：腸内細菌による和漢薬成分の活性化と個人差について –Arctiin の Enterolactone 代謝への個人差. 第 23 回和漢医薬学会大会, 2006, 8, 26-27, 岐阜.
15) 条美智子, 中村憲夫, 垣内信子, 小松かつ子, 服部征雄, 下遠野久美子, 下遠野邦忠, 邱 明華, 酒井伸也, 柴原直利：紫金皮の C 型肝炎ウイルスポリメラーゼ阻害活性について. 第 23 回和漢医薬学会大会, 2006, 8, 26-27, 岐阜.
16) 鄭 美和, 東田道久, 服部征雄：当帰芍薬散の女性ホルモン分泌作用、および関連遺伝子発現変化に関する研究: 卵巣摘出ラットを用いた検討. 第 23 回和漢医薬学会大会, 2006, 8, 26-27, 岐阜.
17) 鈴木佐和子, 鄭 美和, 服部征雄：産後リタイアラットにおける当帰芍薬散のエストロゲン様作用の解明. 第 23 回和漢医薬学会大会, 2006, 8, 26-27, 岐阜.
18) 李 暁宇, 李 仲娟, 高 江静, 並木 崇, 服部征雄, 内山竹彦, 今西健一：霊芝 (*Ganoderma tsugae*) クロロホルム抽出物のマウス免疫系への影響. 第 23 回和漢医薬学会大会, 2006, 8, 26-27, 岐阜.
19) 内山奈穂子, 中村憲夫, 小西天二, 小松かつ子, 服部征雄：タイ民族薬物の抗トリパノソーマ活性. 日本生薬学会第 53 回年会, 2006, 9, 29-30, 埼玉.
20) 鄭 美和, 服部征雄：当帰芍薬散の女性ホルモン分泌作用、および関連遺伝子発現変化に関する研究: 下垂体摘出ラットを用いた検討. 日本生薬学会第 53 回年会, 2006, 9, 29-30, 埼玉.
21) El-Halawany A, M,. Chung M. H., Nakamura N., Nishihara T., Hattori M.: New phenolic constituents of *Cassia tora* seeds and estrogenic activity of same naphthalenes and anthraquinones on ERa and ERb. 日本生薬学会第 53 回年会, 2006, 9, 29-30, 埼玉.
22) El-Dine R. S., Nakamura N., Hattori M.: New lanostane triterpene lactones from the Vietnamise mushroom *Ganoderma colossum*. 日本生薬学会第 53 回年会, 2006, 9, 29-30, 埼玉.
23) 服部征雄, 韓 号峰：健康食品素材としての樟芝菌糸体の薬効評価 –樟芝中性多糖の劇症肝炎にたいする予防効果について–. 第 1 回食品薬学シンポジウム, 2006. 10, 26-27, 大阪.
* 24) Hattori M.: Conversion of naturally occurring lignans to phytoestrogens by anaerobic bacteria. The 2nd International Symposium for Herbal Medicines, 2006, 10, 31, Seoul.
* 25) Hattori M.: Metabolic conversion of some lignans to esterogenic enterodiol and enterolactone by intestinal bacteria. New Thoughts and Approaches to the Future Development of Traditional Chinese Medicine. 2006 Nanjing International Forum on Traditional Chinese Medicine, 2006, 11, 3-5, Nanjing.
26) 鄭 美和：当帰芍薬散の女性ホルモン分泌作用、および関連遺伝子発現変化に関する研究. 日本薬学会北陸支部第 115 回例会, 2006, 11, 12, 富山.
27) 鈴木佐和子, 鄭 美和, 服部征雄.: 経産リタイアラットにおける当帰芍薬散のエストロゲン様作用の解明. 日本薬学会北陸支部第 115 回例会, 2006, 11, 12, 富山.
28) Gao J.: A progressive analytical method for chemically evaluating bitter principles in ganoderma products. 2006 World Congress on Chinese Medicine, 2006, 11, 23-25, Hong Kong.
* 29) Hattori M.: Traditional medicines as sources of antiviral agents. The Conference on Modernization and Internationalization of Chinese Medicine, 2006, 11, 28-29, Taipei, Taiwan.
* 30) Hattori M.: Development of naturally-occurring antiviral agents against herpes simplex, hepatitis C virus and human immunodeficiency virus. The Seventh Joint Seminar, Recent Advances in Natural Product Research and Its Application, 2006, 12, 1-4, Toyama.
31) Wang Z., Ma C., Xiao H., Kakiuchi N., Ota Y., Kita H., Hattori M.: Evaluation of Swertia herbs by LC/DAD/MS. The Seventh Joint Seminar, Recent Advances in Natural Product Research and Its Application, 2006, 12, 1-4, Toyama.
32) Chung M. H., Hattori M.: Stimulating effects of a prescripition Toki-Shakuyaku-San used in Kampo medicine on thalamic-pituitary-gonadal axis in ovariectomized rats. The Seventh Joint

Seminar Recent Advances in Natural Product Research and Its Application, 2006, 12, 1-4, Toyama.

* 33) Hattori M.: Trends of research and education of traditional Oriental medicine in Japan. 2006 Shanghai Forum on International Standardization of Chinese Medicines and Herbal Products, 2006, 12, 10, Shanghai, China.

34) 服部征雄：腸内細菌によるリグナンのエストロゲン様物質への変換. 静岡県立大学 21 世紀 COE プログラム・富山大学 21 世紀 COE プログラム ジョイントシンポジウム「健康長寿に向かう個の医療と薬食同源」, 2006, 12, 13, 東京.

◇その他

1) 服部征雄：きのこを素材とした天然薬物の将来 −古くて新しい資源を考える−. 第 7 回 公開研究報告会, 2006, 3, 19, 富山.
2) 服部征雄：既存添加物の成分と品質評価に関する研究. 厚生労働科学研究費補助金 食品の安心・安全確保推進研究事業 平成 17 年度 総括・分担研究報告書 分冊 その 1 , 2006, 4.
3) 服部征雄：きのこの効用を探る −いま、注目されているきのこ−, 市民公開講座 難波恒雄名誉教授記念講演会, 2006, 9, 24, 於 富山国際会議場.
4) 下遠野邦忠, 服部征雄, 垣内信子, 下遠野久美子：HCV/HIV 阻害活性を有する動植物由来の阻害剤の探索. 財団法人 漢方医薬研究振興財団 研究発表会, 2006. 10, 28, 東京.
5) WFWP2006 女子留学生日本語弁論大会 富山県大会 審査委員長, 2006. 11. 12, 富山.
6) 服部征雄：2006 年度高級技術者派遣, 台湾工研院医所, 於 台湾, 新竹, 2006, 12, 19-23.

◇共同研究

国内

1) 抗 HCV 薬の開発研究　京都大学ウイルス研究所　下遠野邦忠
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2) 腸内嫌気性菌による生薬成分の代謝　富山大学薬学部　赤尾光昭
3) 抗 HSV 薬の開発研究　富山大学医学部　白木公康

◇研究費取得状況

1) 「HCV/HIV 阻害活性を有する動植物由来の阻害剤の探索」漢方医薬研究振興財団（服部分担）50 万円.
2) 「内分泌調節を有する漢方処方−当帰芍薬散・桂枝茯苓丸の脳下垂体に与える影響−」日本科学協会（鄭 美和　代表）54 万円.
3) 「ヒト腸内細菌による植物エストロゲン enterolactone, enterodiol への代謝検討及びその応用」日本科学協会（陳 琮湜　代表）56 万円.
4) 「既存添加物の成分と品質評価に関する研究」厚生労働科学研究費補助金（服部 分担）50 万円.
5) 「消化管をターゲットとした新しい和漢薬製剤の開発研究」富山県（継続、服部 代表）300 万円.

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修士論文：
近藤 直子：乳酸菌によるリグナン類の変換反応の検討（3 月）
大川 美和：C 型肝炎ウイルスポリメラーゼ阻害活性を指標としたタイ民族薬物の探索（3 月）

博士論文：
条 美智子: 中国少数民族薬物の抗単純ヘルペスウイルス作用及び C 型肝炎ウイルス酵素阻害活性について（3 月）
韓 号峰 : Studies on the hepatoprotective substances from the mycelium of *Antrodia cinnamonea*. （3 月）

◇人事異動

馬 超美 : 助教授 (2006. 7. 16 採用)